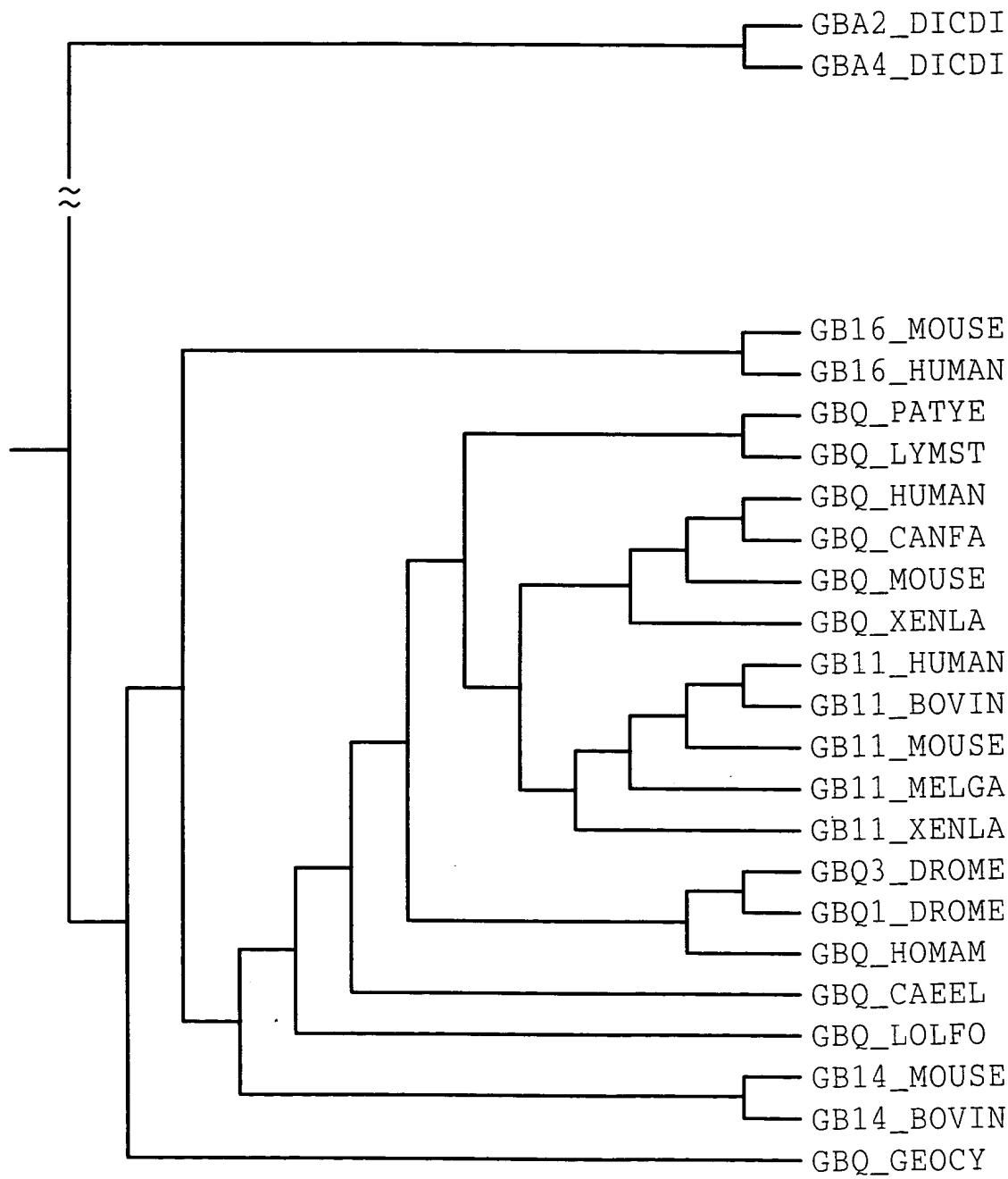


**FIGURE 1**

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*C. elegans*  $G\alpha_{q/z5}$ 

1 MACCLSEEAR EQKRINQEIE KQLQRDKRNA RRELKLLLLG TGESGKSTFI KQMRIIHGQG  
 61 YSEEDKRAHI RLVYQNVFMA IQSMIRAMDT LDIKFGNESE ELQEKAAVVR EVDFESVTSF  
 121 EEPYVSYIKE LWEDSGIQEC YDRRREYQLT DSAKYYLSDL RRLAVPDYLP TEQDILRVRV  
 181 PTTGIIIEYPF DLEQIIFRMV DVGGQRSER R KWIHCFENVT SIMFLVALSE YDQVLVECDN  
 241 ENRMEESKAL FRTIITYPWF TNSSVILFLN KKDLLEEKIL YSHLADYFPE YDGPPRDPIA  
 301 AREFILKMFV DLNPDADKII YSHFTCATDT ENIRFVFAAV KDTILQHNLK **YIGLC**

*C. elegans*  $G\alpha_{q/z9}$ 

1 MACCLSEEAR EQKRINQEIE KQLQRDKRNA RRELKLLLLG TGESGKSTFI KQMRIIHGQG  
 61 YSEEDKRAHI RLVYQNVFMA IQSMIRAMDT LDIKFGNESE ELQEKAAVVR EVDFESVTSF  
 121 EEPYVSYIKE LWEDSGIQEC YDRRREYQLT DSAKYYLSDL RRLAVPDYLP TEQDILRVRV  
 181 PTTGIIIEYPF DLEQIIFRMV DVGGQRSER R KWIHCFENVT SIMFLVALSE YDQVLVECDN  
 241 ENRMEESKAL FRTIITYPWF TNSSVILFLN KKDLLEEKIL YSHLADYFPE YDGPPRDPIA  
 301 AREFILKMFV DLNPDADKII YSHFTCATDT ENIRFVFAAV KDTILQNNLK **YIGLC**

*C. elegans*  $G\alpha_{q/s9}$ 

1 MACCLSEEAR EQKRINQEIE KQLQRDKRNA RRELKLLLLG TGESGKSTFI KQMRIIHGQG  
 61 YSEEDKRAHI RLVYQNVFMA IQSMIRAMDT LDIKFGNESE ELQEKAAVVR EVDFESVTSF  
 121 EEPYVSYIKE LWEDSGIQEC YDRRREYQLT DSAKYYLSDL RRLAVPDYLP TEQDILRVRV  
 181 PTTGIIIEYPF DLEQIIFRMV DVGGQRSER R KWIHCFENVT SIMFLVALSE YDQVLVECDN  
 241 ENRMEESKAL FRTIITYPWF TNSSVILFLN KKDLLEEKIL YSHLADYFPE YDGPPRDPIA  
 301 AREFILKMFV DLNPDADKII YSHFTCATDT ENIRFVFAAV KDTILQMHLR **QYELL**

*C. elegans*  $G\alpha_{q/s21}$ 

1 MACCLSEEAR EQKRINQEIE KQLQRDKRNA RRELKLLLLG TGESGKSTFI KQMRIIHGQG  
 61 YSEEDKRAHI RLVYQNVFMA IQSMIRAMDT LDIKFGNESE ELQEKAAVVR EVDFESVTSF  
 121 EEPYVSYIKE LWEDSGIQEC YDRRREYQLT DSAKYYLSDL RRLAVPDYLP TEQDILRVRV  
 181 PTTGIIIEYPF DLEQIIFRMV DVGGQRSER R KWIHCFENVT SIMFLVALSE YDQVLVECDN  
 241 ENRMEESKAL FRTIITYPWF TNSSVILFLN KKDLLEEKIL YSHLADYFPE YDGPPRDPIA  
 301 AREFILKMFV DLNPDADKII YSHFTCATDT ENIRRVFNDC RDIIQRMHLR **QYELL**

*C. elegans*  $G\alpha_{q/z3(5)}$ 

1 MACCLSEEAR EQKRINQEIE KQLQRDKRNA RRELKLLLLG TGESGKSTFI KQMRIIHGQG  
 61 YSEEDKRAHI RLVYQNVFMA IQSMIRAMDT LDIKFGNESE ELQEKAAVVR EVDFESVTSF  
 121 EEPYVSYIKE LWEDSGIQEC YDRRREYQLT DSAKYYLSDL RRLAVPDYLP TEQDILRVRV  
 181 PTTGIIIEYPF DLEQIIFRMV DVGGQRSER R KWIHCFENVT SIMFLVALSE YDQVLVECDN  
 241 ENRMEESKAL FRTIITYPWF TNSSVILFLN KKDLLEEKIL YSHLADYFPE YDGPPRDPIA  
 301 AREFILKMFV DLNPDADKII YSHFTCATDT ENIRFVFAAV KDTILQHNLK **ECGLY**

***D. melanogaster* G $\alpha$ <sub>q/z5</sub>**

1 MECLSEEAK EQKRINQEIE KQLRRDKRDA RRELKLLLLG TGESGKSTFI KQMRIIHGSG  
61 YSDEDKRGYI KLVFQNIFMA MQSMIKAMDM LKISYGQGEH SELADLVMSI DYETVTTFED  
121 PYLNAAIKTLW DDAGIQECYD RRREYQLTDS AKYLYKDLDR VAQPAYLPTE QDILRVRVPT  
181 TGIIEYPFDL EEIRFRMVDV GGQRSERRKW IHCFENVTSI IFLVALSEYD QILFESDNEN  
241 RMEESKALFR TIITYPWFQN SSVILFLNKK DLLEEKIMYS HLVDYFPEYD GPQRDAITAR  
301 EFILRMFVDL NPDSEKIIYS HFTCATDTEN IRFVFAAVKD TILQSNLK**YI** **GLC**

**FIGURE 3**

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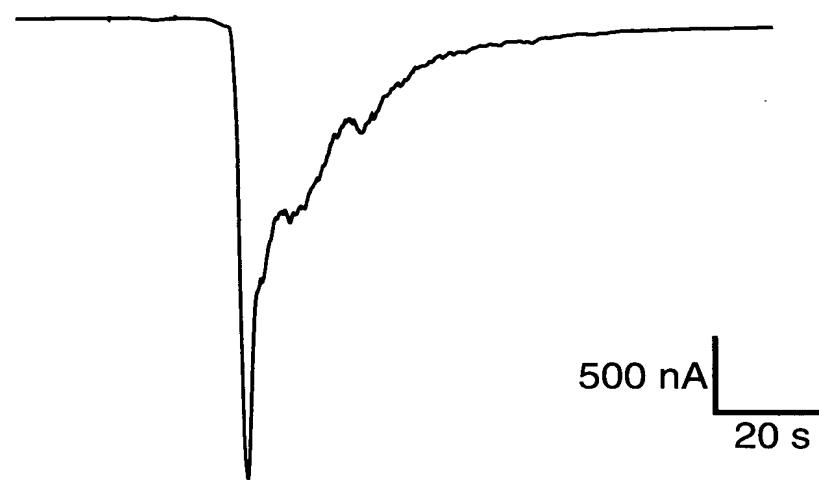
**hNPFF1**

NPFF 1 $\mu$ M



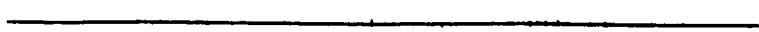
**hNPFF1 + cG $\alpha$ <sub>q/z5</sub>**

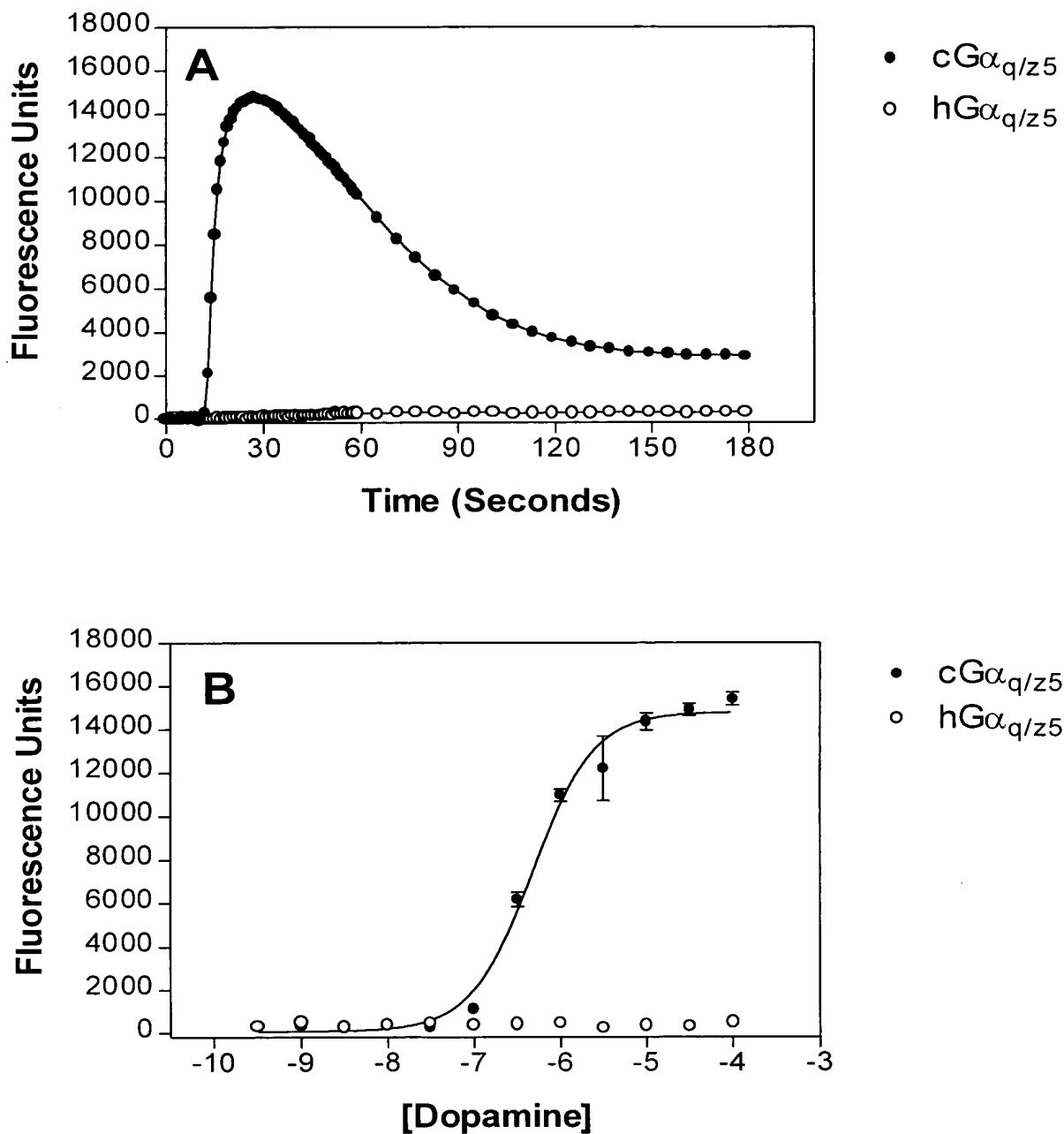
NPFF 1 $\mu$ M



**hNPFF1 + cG $\alpha$ <sub>q/z5</sub>  
+ 190 ng EGTA**

NPFF 1 $\mu$ M



**Human D1**

**FIGURE 5A**

Sequence alignment of GBQ across various species. The alignment shows highly conserved regions marked with asterisks (\*). The sequences are grouped into three blocks, each with a central asterisk and flanking positions 20, 40, 60, 80, and 100.

**Block 1 (Amino acids 1-40):**

GBQ_HUMAN	: MTLESIMACCLSEEAKEARRINDEIE	20	*	40	*
GBQ_CANFA	: MTLESIMACCLSEEAKEARRINDEIE				
GBQ_MOUSE	: MTLESIMACCLSEEAKEARRINDEIE				
GBQ_XENLA	: MTLESIMACCLSEEAEARRINDEIE				
GBQ_PATYE	: ~~~~~MACCLSEEAKEOKRINQEIE				
GBQ_LYMST	: ~~~~~MACCIPDELKEOKRINQEIE				
GBQ1_DROM	: ~~~~~MECCLSEEAKEOKRINQEIE				
GBQ3_DROM	: ~~~~~MECCLSEEAKEOKRINQEIE				
GBQ_HOMAM	: ~~~~~MACCLSEEAKEOKRINQEIE				
GBQ_LIMPO	: ~~~~~MACCLSEEAKEOKRINQEIE				
GBQ_LOLFO	: ~~~~~MACCLSEEAKEOKRINQEIE				
GBQ_CAEEL	: ~~~~~MACCLSEEAKEOKRINQEIE				
GBQ_GEOCY	: ~~~~~MSCLLSEEERLQKRINTRINRE				

**Block 2 (Amino acids 41-100):**

GBQ_HUMAN	: GKSTEFIKQMRIIIHGSGYSDEDKRGFTKLVYONIE	60	*	80	*	100
GBQ_CANFA	: GKSTEFIKQMRIIIHGSGYSDEDKRGFTKLVYONIE					
GBQ_MOUSE	: GKSTEFIKQMRIIIHGSGYSDEDKRGFTKLVYONIE					
GBQ_XENLA	: GKSTEFIKQMRIIIHGSGYSDEDKRGFTKLVYONIE					
GBQ_PATYE	: GKSTEFIKQMRIIIHGSGYSDEDKRGFIKIVYONIE					
GBQ_LYMST	: GKSTEFIKQMRIIIHGAGYSDEDKRSHIKIVYONIE					
GBQ1_DROM	: GKSTEFIKQMRIIIHGSGYSDEDKRGYIKLVFONIE					
GBQ3_DROM	: GKSTEFIKQMRIIIHGSGYSDEDKRGYIKLVFONIE					
GBQ_HOMAM	: GKSTEFIKQMRIIIHGAGYSDEDKRGEIKLVFONIE					
GBQ_LIMPO	: GKSTEFIKQMRIIIHGAGYSDDDKKSYIKLVYONIE					
GBQ_LOLFO	: GKSTEFIKQMRIIIHGSGYSEEDRKGFKEKIVYONIE					
GBQ_CAEEL	: GKSTEFIKQMRIIIHGQGYSEEDKRAHIRLVYONIE					
GBQ_GEOCY	: GKSTEFIKQMRIIIHGKGYSKQDCLEYKNLFRN					

**Block 3 (Amino acids 101-140):**

GBQ_HUMAN	: MKYEHNK--AHAQLREVIVDVEKVS--	120	*	140	*
GBQ_CANFA	: MKYEHNK--AHAQLREVIVDVEKVS--				
GBQ_MOUSE	: MKYEHNK--AHAQLREVIVDVEKVS--				
GBQ_XENLA	: MKYEHNK--GHALLREVIVDVEKVA--				
GBQ_PATYE	: FEVADNE--ENAIIMIROQVYETVT--				
GBQ_LYMST	: YINPANR--ENGNMIRQIDYETVT--				
GBQ1_DROM	: YGQGEHS--ELADLVMSIDYETVT--				
GBQ3_DROM	: YGQGEHS--ELADLVMSIDYETVT--				
GBQ_HOMAM	: YGDSANI--EHADLVRVSDVYESVT--				
GBQ_LIMPO	: YKDRNNI--ENAEELVLSVDYETVT--				
GBQ_LOLFO	: YKDPSN--NEHAEFLNSIDADSAD--				
GBQ_CAEEL	: FGNEEELQEKAAVREVDFESVT--				
GBQ_GEOCY	: YIDPD--AQRHVQLLMALRPETAQ--				

**FIGURE 5B**

	160	*	180	*	200
GBQ_HUMAN :	YDRRRREYQ	-LSDSTKYYLNDLDRVADPAYLFTQQDVLRLVRVPTTGTITIEYP			
GBQ_CANFA :	YDRRRREYQ	-LSDSTKYYLNDLDRVADPAYLFTQQDVLRLVRVPTTGTITIEYP			
GBQ_MOUSE :	YDRRRREYQ	-LSDSTKYYLNDLDRVADPSYLEPTQQDVLRLVRVPTTGTITIEYP			
GBQ_XENLA :	YDRRRREYQ	-LSDSTKYYLNDLDRIAATHGYLFTQQDVLRLVRVPTTGTITIEYP			
GBQ_PATYE :	YDRRRREYQ	-LTDSAKYYLDAVDRIAEPNYLEPTLQDILRVRVMPPTTGTITIEYP			
GBQ_LYMST :	YDRRRREYQ	-LTDSAKYYLDSVERISQQDYLEPTLQDILRVRVMPPTTGTITIEYP			
GBQ1_DROM :	YDRRRREYQ	-LTDSAKYYLSDLARIEQADYLEPTEQDILRARVMPPTTGTITIEYP			
GBQ3_DROM :	YDRRRREYQ	-LTDSAKYYLKDLDRAVQPAYLFTEQDILRVRVMPPTTGTITIEYP			
GBQ_HOMAM :	YDRRRREYQ	-LTDSAKYYLTLDRIAAKDYVSTLQDILRVRVAPPTTGTITIEYP			
GBQ_LIMPO :	YDRRRREYQ	-LTDSAKYYLNDIDRIAVPNYLEPTQQDILRVRVPTTGTITIEYP			
GBQ_LOLFO :	YDRRRREYQ	-LTDSAKYYLDDVERIHEPGYIPTLQDILRVRVMPPTTGTITIEYP			
GBQ_CAEEL :	YDRRRREYQ	-LTDSAKYYLSDLRRLAVPDYLEPTEQDILRVRVMPPTTGTITIEYP			
GBQ_GEOCY :	YQRRNEYQ	-LSDSTKYYLDDLPRISSNDYVETTQDVLRLVRVMPPTTGTINIEYP			
	*	220	*	240	*
GBQ_HUMAN :	FDLQSIVIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_CANFA :	FDLQSIVIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_MOUSE :	FDLQSIVIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_XENLA :	FDLQSIVIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_PATYE :	FDLDSIIIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_LYMST :	FDLDSIIIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ1_DROM :	FDLDGIVIFRMVDVGGQRSERKWIHC	CFENVTSTIIFIVAFSEYDOILF	ESD		
GBQ3_DROM :	FDLLEEIRIFRMVDVGGQRSERKWIHC	CFENVTSTIIFIVAFSEYDOILF	ESD		
GBQ_HOMAM :	FDLLEEIRIFRMVDVGGQRSERKWIHC	CFENVTSTIIFIVAFSEYDOILF	ESD		
GBQ_LIMPO :	FDLDSIIIFRMVDVGGQRSERKWIHC	CFENVTSTIIFIVAFSEYDOILF	ESD		
GBQ_LOLFO :	FDLYSIIIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_CAEEL :	FDLEQIIIFRMVDVGGQRSERKWIHC	CFENVTSIMFLIVAFSEYDOVLV	ESD		
GBQ_GEOCY :	FTINKIIFKMDVGGQRSERKWIHC	FDHVTSMFIVAFSEYDOILV	EA		
	260	*	280	*	300
GBQ_HUMAN :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ_CANFA :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ_MOUSE :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ_XENLA :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ_PATYE :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMHSHLVDYF			
GBQ_LYMST :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMHSHLVDYF			
GBQ1_DROM :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ3_DROM :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ_HOMAM :	N-ENRMEESKALFR	RTIITYPWFQHSSVILFLNKEDLIEEKIMYSHLVDYF			
GBQ_LIMPO :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMFSHLVDYF			
GBQ_LOLFO :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKIMTSHLADYF			
GBQ_CAEEL :	N-ENRMEESKALFR	RTIITYPWFQNSSVILFLNKEDLIEEKILYSHLADYF			
GBQ_GEOCY :	SRVNRMVESLHLFNTISYPWFNKSSI	ILFLNKEDLIEEKVMHSHLIDYF			

## FIGURE 5C

		*	320	*	340	*
GBQ_HUMAN	:	PEYDGPQRDAQAAREFTEKMFVDLNPESDKIITYSHFTCATDTENIRREVFA				
GBQ_CANFA	:	PEYDGPQRDAQAAREFILKMFVDLNPESDKIITYSHFTCATDTENIRREVFA				
GBQ_MOUSE	:	PEYEGPQRDAQAAREFILKMFVDLNPESDKIITYSHFTCATDTENIRREVFA				
GBQ_XENLA	:	PEYDGPQRDAQAAREFTEKMFVDLNPESDKIITYSHFTCATDTENIRREVFA				
GBQ_PATYE	:	PEFDGOKKDAQGAREFILRMEVDLNPDPDKIITYSHFTCATDTENIRREVFA				
GBQ_LYMST	:	PEFDGPKKEASTAREFILKMFVELNPDPDKIITYSHFTCATDTENIRREVFA				
GBQ1_DROM	:	PEYDGPQKDHAAKQFVKKYLACNPDPEROCYSHETTATDTENIKLVFC				
GBQ3_DROM	:	PEYDGPQRDAITAREFILRMFVDLNPSEKIIYSHFTCATDTENIRREVFA				
GBQ_HOMAM	:	PEYDGPRKDAIAAREFILRMFVELNPDPERKITYSHFTCATDTENIRREVFA				
GBQ_LIMPO	:	PEYDGPKKDAVOGREFTEKMFVDLNPSEKIIYSHFTCATDTENIRREVFA				
GBQ_LOLFO	:	PDYDGPKCDYEAAREFMMDSYMDLNEEKMLYYHYTCATDTENIRREVFA				
GBQ_CAEEL	:	PEYDGPRLDPIAAAREFTEKMFVDLNPPLADKITYSHFTCATDTENIRREVFA				
GBQ_GEOCY	:	EEYDGPKCDHVSARESTAKMEFISINDMRSADLYPHFTCATDTENIKEVFD				
			360	*		
GBQ_HUMAN	:	AVKDTIIEQLNLKEYNAV~~~			359	
GBQ_CANFA	:	AVKDTIIEQLNLKEYNLV~~~			359	
GBQ_MOUSE	:	AVKDTIIEQLNLKEYNLV~~~			359	
GBQ_XENLA	:	AVKDTIIEQLNLKEYNLV~~~			359	
GBQ_PATYE	:	AVKDTIIEQLNLKEYNLV~~~			353	
GBQ_LYMST	:	AVKDTIIEQLNLKEYNLV~~~			353	
GBQ1_DROM	:	AVKDTIMONALKEEFDIG~~~			353	
GBQ3_DROM	:	AVKDTILOSNLKEYNLV~~~			353	
GBQ_HOMAM	:	AVKDTIIEQLNLKEYNLV~~~			353	
GBQ_LIMPO	:	AVKDTIIEQLNLKEYNLV~~~			353	
GBQ_LOLFO	:	AVKDTIIEQLNLKEYNLV~~~			354	
GBQ_CAEEL	:	AVKDTIIEQHNEKEYNLV~~~			355	
GBQ_GEOCY	:	VVKNHILOOHITE--VVPGL			355	